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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,064	10/05/2005	Oliver Schadt	MERCK-3067	6539

23599 7590 09/26/2007

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EXAMINER	
JARRELL, NOBLE E	
ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
09/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,064	SCHADT ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Current Status of 10/552064

1. The restriction dated 3/14/2007 was made FINAL in the office action dated 5/14/2007.

2. The rejection under 35 USC 112 2nd has been overcome by the amendment filed 8/7/2007.

3. The provisional rejection on the ground of non-statutory obviousness type double patenting has been overcome by the terminal disclaimer filed 8/7/2007.

4. Currently claims 1-13 and 15-22 are pending. The same claims are examined on the merits in the instant application.

5. The foreign priority document, DE 103151569, is provided as a courtesy copy for applicants.

Rejections based on amended claims

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-13 and 15-22 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of the parent compounds of formula I, does not reasonably provide enablement for the solvates of the compounds of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification adequately shows the preparation of compounds 1-703. However, applicants are not enabled for the solvates of these compounds. The formation of solvates is unpredictable (Vippagunta et al. *Advanced Drug Delivery Reviews*, **2001**, *48*, 3-26).

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds with core comprising pyrazole connected to pyridine or benzene, depending on what group variable R^1 is.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Vippagunta et al. state (page 18, section 3.4): "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult." Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds."

(5) The relative skill of those in the art:

One of ordinary skill in the art is a chemist who is familiar with the synthetic procedures shown in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the preparation of parent compounds of claim 1.

However, the specification does not provide guidance for the formation of solvates.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-13 and 15-22 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

8. Claims 11 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the disorders cited in claim 16, does not reasonably provide enablement for the prevention of the disorders in claim 16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The treatment of each disorder in claim 16 is enabled because each disorder has a direct relationship to 5-HT receptor modulation. However, none of the disorders listed in claim 16 can be prevented. When one sees the term "prophylaxis", one assumes that a disorder can be cured or prevented. Claims 11 and 16 are directed (in part) toward the prophylaxis of a 5-HT mediated disease and the prevention of each disease in claim 16.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However,

experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to the treatment and/or prevention of 5-HT mediated disorders.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Premenstrual syndrome has no cure, and therefore is not preventable ("Premenstrual syndrome-Womens health and Medical Information in Medicinenet.com", http://www.medicinenet.com/premenstrual_syndrome/page5.htm, accessed September 19, 2007).

Amyotrophic lateral sclerosis has no cure as well ("Amyotrophic Lateral sclerosis information page: National Institute of Neurological Disorders and Stroke (NINDS)", http://www.ninds.gov/disorders/amyotrophiclateralsclerosis/amyotrophiclateralsclerosis.htm, accessed September 19, 2007).

Obsessive-compulsive disorder is not preventable ("Obsessive-compulsive behaviors and disorders: symptoms, treatment, and support", http://www.helpguide.org/mental/obsessive_compulsive_disorder_ocd.htm, accessed September 19, 2007).

Not all neurological disorders are preventable. One example of a neurological disorder is Alzheimer's disease. Pulley et al. (US 7,067,507, issued June 27, 2006) state (column 2,

lines 40-45): At present there are no effective treatments for halting, preventing, or reversing the progression of Alzheimer's disease."

Not all psychoses have a cure. Schizophrenia, one psychosis is not preventable (*Journal of Clinical Psychiatry*, **1999**, *60*, 1-8)(page 3, under "Medication during the recovery period" heading).

Eating disorders are not preventable because the cure/prevention of an eating disorder requires much more than a single compound (Crow, S. *Expert Opinion on Investigational Drugs*, **1997**, *6(4)*, 427-36, "future directions" section).

(5) The relative skill of those in the art:

One of ordinary skill in the art is familiar with *in vitro* methods of testing activity against 5-HT receptors.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the treatment of disorders in claim 16.

However, the specification does not provide guidance for the cure of disorders listed in claims 11 and 16.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 11 and 16 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Double Patenting

9. Claim 19 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

10. Claim 21 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 7. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/551998.

Although the conflicting claims are not identical, they are not patentably distinct from each other because compound 6 (page 9) in 10/551998 can be embraced by claim 1 in both applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 3, 6, 10, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Bamaung et al. (US20010044445, published November 22, 2001). Bamaung et al. teach structure (xxiv)-a A (pages 28 and 34: structure shown on page 28 and meaning of variables on page 34). In this structure, variables (of the instant claims) X, R^1, R^2, and R^4 are N, NO_2, CF_3, and CF_3 ((CH_2)n-Het where n is 0 and het is an alkyl chain substituted with three hal groups).

15. Claims 1,4,6-8, 10,19, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Beck (US 4631343, issued December 23, 1986). Beck teaches example 13 (column 11, lines 30-33), which has the following meanings for variables R^1, R^2, X and A: chloro (halogen), cyano ($(CH_2)_n$Het), N, and ethyl. Each of these groups is valid for each of the claims. Formula IA of claims 7 and 21 is anticipated by this structure. Claim 8 is anticipated because of the synthetic scheme depicted in column 6.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

18. Claims 1, 4-7, 19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schiemann et al. (WO 03/031435, published 17 April 2003). Schiemann et al teach structure 9 on page 26, which has the following meanings for variables R^1, R^2, X and A: benzene, 2-fluorophenyl, CH, and ethyl. This compound is a positional isomer of the claimed compounds because the nitrogen atom is three atoms away from the pyrazole ring. In the same reference (in the abstract) it is stated that these compounds are being used to treat various neurodegenerative disorders (Alzheimer's disease, Lewy bodies dementia) and psychotic disorders (schizophrenia). The motivation for using compound 9 is that it can be used for the same claimed purpose as the instant invention, and the only difference is the position of the N in the pyridine ring. Thus, claims 1, 4-7, 19, and 21 are rendered unobvious over Schiemann et al.

Allowable Subject Matter

19. No claims are allowable.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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